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Synchrotron X-Ray Footprinting of the Ca^{2+} Activated Structure of the Human Plasma Gelsolin Protein as a Function of Ca2+ Concentration

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ABSTRACT: Gelsolin is a calcium-dependent actin regulatory protein that severs actin filaments and caps the fast-growing barbed end with high affinity. Spectroscopic analysis shows that nannomolar calcium induces a large conformational transition that is appears to “unlatch” the interface connecting domains 2 and 6, thus exposing sites essential for actin binding. A combination of synchrotron radiolysis and mass spectrometry are applied to study the calcium-induced structural changes in gelsolin. Hydroxyl radicals, produced by radiolysis with synchrotron radiation, result in the efficient oxidation of aromatic and sulfur-containing amino acids of gelsolin protein in proportion to their solvent accessibility. The rate of oxidation at these sites is quantitatively measured by mass spectrometry. Upon Ca2+ activation a number of amino acids in gelsolin undergo substantial changes in solvent accessibility, and we predict that these gelsolin residues will have different rates of oxidation in the absence and presence of Ca^{2+}. Additionally synchrotron x-ray footprinting can be applied to examine the nature and conformational dynamics of gelsolin-actin complex. Actin bound to the surface of gelsolin will afford a degree of protection from oxidation at the reactive residues to enable the binding site to be identified.